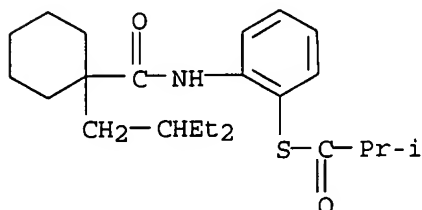


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L6 ANSWER 1 OF 1 ADISINSIGHT COPYRIGHT (C) 2006 Adis Data Information BV on  
STN  
AN 2000:1688 ADISINSIGHT  
SO Adis R&D Insight  
DN 014840  
CDAT Oct 26, 2004  
CN JTT 705  
CN R 1658  
CN S-(2-(((1-(2-ethylbutyl)cyclohexyl)carbonyl)amino)phenyl)propanethioic  
acid, 2-methy-,  
MF C23 H36 N O2 S  
RN 211513-37-0  
STR



CC EPHMRA ATC CODE: C10A9 All other cholesterol/triglyceride regulators  
CC WHO ATC CODE: C10A Cholesterol and Triglyceride Reducers  
HDP Phase II  
DSTA Phase II, Netherlands, Hyperlipidaemia  
Phase II, Unknown, Hyperlipidaemia  
Phase I, Japan, Hyperlipidaemia  
ORIGINATOR: Japan Tobacco (Japan); Japan Tobacco (Unknown)  
PARENT: Japan Tobacco  
LICENSEE: Roche  
OS 800911674  
WC 329

## TX TEXT

## Introduction:

JTT 705 (R 1658), a thioester, is a potent cholesteryl ester transfer protein (CETP) inhibitor being developed by Japan Tobacco to slow or prevent atherosclerosis. CETP is a plasma glycoprotein that mediates the transfer of cholesteryl ester from high density lipoprotein cholesterol (HDL) to proatherogenic very low density lipoprotein cholesterol (VLDL) and LDL.

## Company agreements

In October 2004, Japan Tobacco and Roche entered into a licensing agreement for the development and commercialisation of JTT 705. Japan Tobacco will retain rights in Japan and Korea and receive milestone payments and royalties from Roche for exclusive rights to the rest of the world/1/.

## Key development milestones

Phase I trials in Japan and phase II trials in the Netherlands and other unspecified countries, have been reported in patients with hyperlipidaemia.

TX PHARMACOLOGY OVERVIEW:  
Antimicrobial activity:

Pharmacodynamics:

Attenuates atherosclerosis in cholesterol-fed rabbits  
Mechanism of action:  
Cholesteryl ester transfer protein antagonists

TX CLINICAL OVERVIEW:

Route(s) of Administration: PO

Drug Interactions:

Unknown.

TX Adverse Events:

JTT 705, at dosages of 300, 600 and 900 mg/day, was well tolerated in patients with hyperlipidaemia. Digestive complaints occurred in 21, 25 and 27% of 300, 600 and 900 mg/day recipients, and 12% of placebo recipients/2/.

TX PHARMACOLOGY:

Pharmacodynamics (Hyperlipidaemia):

Preclinical studies: JTT 705 attenuated atherosclerosis in cholesterol-fed rabbits according to the results of a study conducted in Japan. In this study, rabbits were given a cholesterol-containing diet alone to establish hyperlipidaemia, then JTT 705 or simvastatin was added to the diet for 6 months. Compared with untreated controls, JTT 705 and simvastatin recipients had HDL-cholesterol levels which were 90 and 28% higher, respectively, and non-HDL-cholesterol levels which were 40-50 and 50-70% lower, respectively. Compared with controls, the area of atherosclerotic lesions in the aortic arch was 70% lower in JTT-705 recipients and 80% lower in simvastatin recipients/3/.

JTT 705 demonstrated 95% inhibition of cholesteryl ester transfer protein, a protein that transfers neutral lipids among lipoproteins, in JW rabbits/4/.

Clinical studies: after 4 weeks, JTT 705 at dosages of 300, 600 and 900 mg/day, had increased high density lipoprotein cholesterol levels ( $p \leq 0.001$ ), and decreased cholesteryl ester transfer protein activity ( $p \leq 0.001$ ) in patients with hyperlipidaemia/2/.

RDAT

RNTE

26 Apr 2002	Phase-II clinical trials in Hyperlipidaemia in Netherlands (PO)
01 Nov 2000	New profile
01 Nov 2000	Phase-I clinical trials for Hyperlipidaemia in Japan (Unknown route)
01 Nov 2000	Phase-II clinical trials for Hyperlipidaemia (Unknown route)

RE

1. Japan Tobacco Inc, Roche. Roche and Japan Tobacco Enter Agreement for Novel Cholesterol Modifying Agent. Media Release. : 20 Oct 2004. Available from: URL: <http://www.rocheusa.com>. (English).
2. Kuivenhoven JA, Stalenhoef AFH, et al. Efficacy and safety of a novel cholesteryl ester transfer protein inhibitor, JTT-705, in humans: a randomized phase II dose-response study. Circulation. 105: 2159-2165, 7 May 2002. (English). 800911674
3. Maeda K, Minowa T, et al. A cholesteryl ester transfer protein inhibitor attenuates atherosclerosis in rabbits. Nature. 406: 203-207, 13 Jul 2000. (English).
4. Maeda K, Okamoto H, et al. Bis(2-(acylamino)phenyl) disulfides, 2-(acylamino)benzenethiols, and S-(2-(acylamino)phenyl) alkanethioates as novel inhibitors of cholesteryl ester transfer protein. Journal of Medicinal Chemistry. 43: 3566-3572, 21 Sep 2000. (English).

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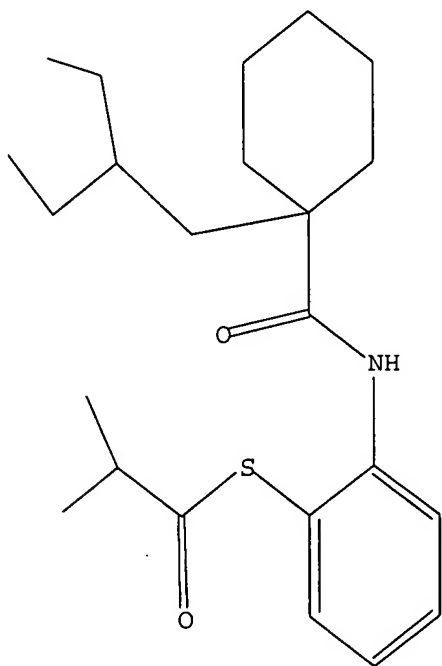
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Structure attributes must be viewed using STN Express query preparation.